

DATE: April 22, 1975

To

FROM Joshua Lederberg
Department of Genetics

SUBJECT: Draft Proposals for Research Bearing on Water Reclamation

I am very grateful for the opportunity to have participated in the meeting last Friday and wish it had been possible for me to attend the entire session. I look forward to seeing the minutes of the further proceedings.

I was glad to see that there was no lack of appreciation of the complexity of the problem of toxicity evaluation of substances that may be found in water supplies and the additional burden on that list that reclamation processes will undoubtedly entail.

One way of expressing this point is to recall that under current FDA regulations new products must undergo on the average from \$1 million to \$3 million of safety testing before a new drug entity can be marketed. (This is apart from other costs connected with proving the efficacy of the new agent). Since it is clear that there will be many thousands of chemical substances in our water supplies that can be detected by modern sophisticated analytical techniques and potentially many hundreds of thousands of others that could be found if we push these methodologies to their ultimate possibility of sensitivity, it should be perfectly obvious how futile it would be to attempt an evaluation of the safety of additives to water supplies along the same lines as are now imposed for the definition of new drugs and food additives. We are, of course, dealing with somewhat different kinds of problems in the sense that our problems with water supplies have to do with the extremely broad dissemination of substances in trace amounts even by contrast to the analogous problem with food additives and the more so with respect to drug entities. This suggests that we must develop alternative strategies of environmental surveillance that are far more sensitive to questions of quantitative risk assessment and to the issues of chronic effects at low dose even than pertain to the other areas of safety regulation. With the exception of a few selected high priority targets our research will simply be unable to deal with each entity one at a time. Consider how difficult it is already to find reasonable standards for specific identifiable substances already known to be in many water supplies like chloroform and asbestos where it is obvious that no one has the foggiest idea what possible bounds of hazard may be reflected in existing circumstances.

It seems to me then that our recommendations for research programs must be focussed at a number of different levels: including even a deeper analysis of the research strategy itself, so that what will inevitably be an insufficient number of dollars to do the job properly may nevertheless give us the best result still achievable.

over

At level one I have in mind the improvement of our overall methodology of risk assessment of environmental chemicals. Most laymen do not have the foggiest idea what a quandary we are in in trying to obtain useful estimates of human risk in a toxicological framework. We urgently need great improvements in our general insight into questions like the variability of individual human response to a variety of chemicals; the mathematical form of dose-risk curves; the techniques for extrapolation from animal experimentation at high levels to the assessment of human population risks. Whatever possibility there may have been with respect to the attitude of demanding absolute safety and zero risk with respect to intentional chemical additives, we do not have that luxury with respect to our water supplies; and we must learn to develop policies based on optimum risk rather than the fantasy of zero risk. This is no longer a question of imposing economic burdens on one particular category of producers or innovators but an area of shared risk in which the entire community must inevitably participate. There is no economically or socially feasible way in which water supplies can be furnished to the public that consist of absolutely pure water to the total exclusion of other material - even fresh rain water or highly purified distilled water will still contain detectable amounts of other constituents. And as soon as we have human congregations, the contamination of water supplies with potentially contagious agents, not to mention chemical additives, is absolutely inevitable. If this objective fact is not widely understood, the further pursuit of water hygiene will be founded on a pernicious fallacy.

A second level of investigation is undoubtedly already given considerable impetus judging from recent news reports; and this should concern the development of chemical methodology and the survey of existing water supplies for the actual prevalence of observable chemical species in different regions of the country. Our primary mission is the assessment of water reclamation, but we can hardly adopt as a standard for reclaimed water criteria that ignore the ambient situation with respect to existing water supplies. We should keep in mind, however, that there is likely to be increasing pressure (1) towards the achievement of even higher standards of safety for such primary water supplies, but (2) increasing economic pressure in the opposite direction. These may become more and more important in the future if we are to assess the ultimate projection of the role of reclaimed water in future policy.

Hopefully information on the abundance of organic and inorganic contaminants may enable us to seek out a number of specific high priority targets for more specific toxicity evaluation. For example, the recent findings of the abundance of chloroform as an ultimate residue from the interaction of chlorine with a variety of organic inputs obviously points to the need to reassess the chronic toxicity of chloroform at rather low concentrations but distributed to the entire population. The fact that large doses are capable of inducing liver damage and liver nodules in rodents is only a primary alarm and is hardly a secure basis for undertaking costly and possibly futile measures to eliminate chloroform from our water supplies. This will not be an easy task but certainly the first steps that need to be undertaken are chronic feeding studies to animals at various levels of chloroform intake. Connected with this should be a very careful analysis of the biochemical and physiological pathways by which chloroform exerts its toxic effect since it is unlikely that empirical measurements alone can be extrapolated to give us reliable information on the impact of parts per million levels of contamination. (My view is that a judicious combination of

empirical research on dose-toxicity relationships and of more basic theoretical studies on the mechanism of toxic action are indispensable for extrapolations of chronic toxicity measurements down to the level of expected human exposure!)

If there are more than a dozen or so chemical species that become highly suspect owing to their prevalence in water supplies, we will face an almost impossible level of cost in endeavoring to find really credible answers to the questions posed by their potential toxicity.

Another level of search should therefore be poised at more global rather than selective methods of toxicity evaluation of water additives. When we think of chronic long-term effects, a large part of our concern is directed to potential carcinogenesis. Fortunately through the work of Bruce Ames and others we have increasing confidence about the useful role of simplified microbiological test-systems for guessing at the average carcinogenic potential of a range of chemicals. This is an approach that has already been applied to a number of single chemical species although we do not yet have a good calibration that enables us to make reliable quantitative estimates of human risk from bacterial experiments and this is certainly one of the lines of investigation that needs to be pursued. However, even failing that, one could envisage the development of practical test protocols that involve the extraction of a significant fraction of the organic load from a water supply, the elution of these materials from the adsorbent, and the testing of these concentrates for mutagenic activity in bacterial test-systems. Certainly, water supplies that gave fluctuating responses in such assays would be candidates for suspicion and for aggressive pursuit of the individual culprits in question. This approach bids fair to shorten the efforts that would be involved in some global assessment of organic chemical aspects of water quality since it would not necessarily involve the isolation of hundreds of different chemical entities as the first step in the analysis. Rather, this would wait upon the finding of a suspicious positive result.

These experiments would be directed at the assessment of the toxic load of a water supply before the final purification process, as an index of the possible leakthrough even after purification by adsorption had been allowed to run its course.

Plainly, another very important arena for further research is the thorough practical and theoretical analysis of the adsorption process itself. We can hardly afford to rely on the hope that a given specimen of charcoal will be universally effective in removing all organic chemical constituents with equal efficacy and with unflagging efficiency throughout the cycle of use of the material. We need far more sophisticated models of the adsorption process that take account of the role of the competition between different chemical species, the saturation of adsorbing sites by one compound as it may influence the efficiency of adsorption of others, the development of indexes and assays to monitor the efficiency of adsorption and so forth. With such information we will be in a position to make theoretical estimates of the level of effective filtering out of undesirable chemical species by a given process and we will be in the position of conducting our analysis on the influent which is far more amenable to chemical analytical procedures than the effluent after purification. In the process we may also hope to understand adsorbency to the point of being able to design ever more efficacious agents, processes and protocols for use and for monitoring.

Such studies may reveal which compounds may safely be allowed to enter into water supplies destined for eventual reclamation, and which will have to be monitored closer to their proximate source. We may then wish to do investigations at still another level, of social engineering, for example to determine the feasibility of taxing the producers of specific effluents in some relation to the cost of their removal. This would also imply monitoring at the principal sources of novel effluents - here I have in mind special chemical industries which introduce a still new variety of chemical entities into the water supply - a monitoring that is likely to be more efficacious at the source than after admixture with the total water supplies. Furthermore, the knowledge of specific sources of contamination gives us specific and detailed information about the characteristics of chemical entities that would be difficult to decipher in the global pool.

In addition I think that special emphasis does have to be given to the chemistry and biological consequences of a process like chlorination since this is such a fundamental part of our overall strategy of water protection and since chlorination has by now been amply demonstrated to be the source of an abundant variety of new and sometimes unexpected chemical species of potential toxicity. In a sense the use of chlorine has converted natural products like the humic acids into an industrial effluent. The study of these reactions with chlorine may enable us more intelligently to single out individual high priority candidates for selective toxicity analysis. In addition, chlorinated derivatives are quite likely to be among those which are the least biodegradable and therefore may play a significant role in the problem of water buildup in the context of studies on reclamation.

All of these problems will have their comparable analogues even if chlorination were to be replaced by other methods of water disinfection.

To the extent that reclaimed water poses new biological as well as chemical burdens, we may have to anticipate other kinds of interaction that need to be taken account of in our overall strategy. For example, if chlorination must be relied upon to a greater degree as a means of coping with the contaminants present in reclaimed water, then this must be regarded as one of the costs of reclamation as opposed to primary water usage.

Besides the products of chlorination reactions that have been identified in potable water as distributed, we have also to consider the further products of chemical reaction of residual chlorine with dietary and physiological constituents. And then we have to consider not only natural dietary constituents and bodily secretions but also additives that are being evermore widely used in increasing amounts. Part of the safety evaluation of materials like cyclamates and saccharin will have to include their interaction with chlorine to the extent that this remains chemically active at the point of admixture and human intake. This is a problem that can hardly be ignored with respect to primary water supplies subject to chlorination but is likely to achieve even greater prominence to the extent that reclaimed waters may require further disinfection.

The previous discussion focussed on the chemical hazards relevant to water supply and reclamation. For assessing biological hazards, we also need substantial new information particularly with respect to the survival of viruses. Fortunately, in the operation of domestic septic tanks we already have some traditional usage that may be relevant to this problem but which may require re-examination from a fresh outlook. Certainly we need to know much more about the survivability of different microbial and viral species in the actual circumstances of aquifer replenishment and other modes of recirculation. As I discussed at the meeting, we can hardly rely in any quantitative way on existing indices of coliform survival as measures of the effective level of fecal pollution. The most troublesome point is of course the possible durability of some microbial and many viral species which might allow for very substantial build-up and broadcasting of infectious agents through the reclamation route.

Segregated water supplies may be an avenue of solution especially for chemical contamination, but even this must be validated by more experimental work on the extent to which agricultural products are in practice contaminated by additives in irrigation water. Of course, details of agricultural practice may have a lot to do with the extent to which contaminating materials, chemical or biological, find themselves in the final edible product. I do not know whether there had been studies on the uptake of infectious agents like hepatitis virus through the roots of growing plants, and of course each chemical entity must have rules of its own with respect to the possibility of chemical concentration in the food cycle. One of the hazards of supply segregation is that water supplies that would be kept at a level of marginal potability under a non-segregated regime may allow to become heavily contaminated in a nonchalant fashion with possibly very dangerous results.

Since wastes must eventually end up in the oceans, whether they go through a reclamation cycle or not, we should not entirely avoid the questions of the adequacy of the oceanic reservoir - the effects on marine life and eventually on water quality and other environmental values of the same chemical constituents about which we are concerned in a water reclamation context. The chlorinated hydrocarbon insecticides already give us a notorious precedent to illustrate this point. I am not suggesting that I believe that there is a crisis of planetary habitability looming within the next 25 years, as some of my fellow biologists have suggested, but it is not too soon to be applying the same kind of concern that we express about our own fresh water supplies to an oceanic context.